

Human Papillomavirus and Penile Cancer

EDITORIAL COMMENT

This study is very welcome as it demonstrates the high rate of human papillomavirus (HPV) associated with penile cancer. The detection rate of 75% approaches the rate of 90% seen in carcinoma in-situ. Other studies show lower HPV rates. It was unclear if this was due to differences in technique, such as immunohistochemistry or due to real variations in biology. Furthermore, the lower rate of HPV (50%) in verrucous type indicates a possible different etiology to this subset of cancer. Studying the subtypes of HPV associated with penile cancer is paramount currently, given the recent development of vaccines against specific subtypes of HPV. It is hard to project the effect mass vaccination of females will have on males, but ought to reduce carriage of HPV among heterosexual males. Vaccinating males may have benefits for females also, as total immunization of the whole female population is unlikely. Reduc-

ing the overall population pool of these subtypes is likely to benefit both males and females. The impact on the incidence and type of penile cancer is likely have a lead time of several decades, as only a quarter of men with penile cancer present under the age of 50. Projections must also take into account the increasing life-expectancies in developed countries with more men living into their 70s and 80s, where the disease is more prevalent (see [http:// www.oecd.org/statsportal/](http://www.oecd.org/statsportal/)). Thus in the absence of any vaccination the prevalence is likely to increase, whereas even with successful vaccination changes in demographics may reduce the benefit in the initial years. Finally, the subtypes of HPV being targeted may result in only some cancers being prevented. These factors must be brought together in modeling and scenario planning when formulating strategies for service provision in any healthcare system.

Dr. P. K. Hegarty

*Institute of Urology and Pathology
University College Hospital London
London, UK
E-mail: Paulhego@hotmail.com*

EDITORIAL COMMENT

The prevalence of penile cancer in Brazil is 2% and this is higher than in the USA and Europe, where it accounts for 0.3 to 0.6% of cancers (1,2). Squamous cell carcinoma (SCC) is the most common histological type of penile cancer and represents 95% of cases. However the aetiology of penile cancer is unknown, risk factors include age and lack of circumcision (1,2). Other predisposing factors to the development of penile SCC are the chronic inflammatory disorder penile lichen sclerosus (LS) (also termed balanitis xerotica obliterans) (3-6) or human papillomavirus (HPV) infection (1,2,7,8). A common aetiology for penile and cervical cancer is suggested by the geographical correlation between the incidence of penile

and cervical cancers worldwide (9). The persistent infection with sexually transmitted high risk HPV is the main cause of cervical cancer (10,11). The prevalence of HPV penile infections in healthy men is reported to be 39% in Brazil and 3-9% in Western Europe, where there is a lower incidence of penile cancer (12,13). However, HPV detection in penile cancer cases varies from 20-80%, depending on detection method and geographical location (1,2). This is unlike cervical cancer where HPV infection can be detected in almost all cases (10).

The paper entitled "Human Papillomavirus and Penile Cancers in Rio de Janeiro, Brazil: HPV Typing and Clinical Features" concerns penile cancer HPV infection and survival in 80 consecutive

cases of patients who underwent surgery at Hospitals in Rio de Janeiro between 1995 and 2000. High risk HPV 16 was the predominate HPV type detected and no correlation was observed between HPV status (all types) and penile cancer subtype, stage, regional metastases or survival. HPV 16 has previously been reported to predominate in penile lichen sclerosus and SCC and may be an aetiological agent in the development of a significant proportion of penile cancers (7,14). However the importance of HPV status in penile cancer progression and patient survival is controversial, as high-risk HPV is associated with aggressive variants (8) but recent series examining the relationship of HPV infection with prognosis have revealed either no correlation survival or a favourable survival (15,16). This study from Rio de Janeiro is consistent with only inguinal metastasis being a prognostic factor for penile cancer survival. In summary, high risk HPV infection occurs in penile SCC and it is likely to be an aetiological agent in the development of a significant proportion of penile cancers. These results are important as prophylactic HPV vaccines for prevention of cervical cancer in women could also prevent penile cancers in men. However, several studies, including this one, show that once penile cancer has developed poor prognosis is associated with the occurrence of lymph node metastasis and not HPV status.

REFERENCES

1. Micali G, Nasca MR, Innocenzi D, Schwartz RA: Penile cancer. *J Am Acad Dermatol.* 2006; 54: 369-91.
2. Kayes O, Ahmed HU, Arya M, Minhas S: Molecular and genetic pathways in penile cancer. *Lancet Oncol.* 2007; 8: 420-9.
3. Nasca MR, Innocenzi D, Micali G: Penile cancer among patients with genital lichen sclerosus. *J Am Acad Dermatol.* 1999; 41: 911-4.
4. Depasquale I, Park AJ, Bracka A: The treatment of balanitis xerotica obliterans. *BJU Int.* 2000; 86: 459-65.
5. Powell J, Robson A, Cranston D, Wojnarowska F, Turner R: High incidence of lichen sclerosus in patients with squamous cell carcinoma of the penis. *Br J Dermatol.* 2001; 145: 85-9.
6. Pietrzak P, Hadway P, Corbishley CM, Watkin NA: Is the association between balanitis xerotica obliterans and penile carcinoma underestimated? *BJU Int.* 2006; 98: 74-6.
7. Prowse DM, Ktori EN, Chandrasekaran D, Prapa A, Baithun S: Human papillomavirus-associated increase in p16INK4A expression in penile lichen sclerosus and squamous cell carcinoma. *Br J Dermatol.* 2008; 158: 261-5.
8. Gregoire L, Cubilla AL, Reuter VE, Haas GP, Lancaster WD: Preferential association of human papillomavirus with high-grade histologic variants of penile-invasive squamous cell carcinoma. *J Natl Cancer Inst.* 1995; 87: 1705-9.
9. Parkin DM, Bray F: Chapter 2: The burden of HPV-related cancers. *Vaccine.* 2006; (Suppl 3): S11-25.
10. zur Hausen H: Papillomaviruses and cancer: from basic studies to clinical application. *Nat Rev Cancer.* 2002; 2: 342-50.
11. de Villiers EM, Fauquet C, Broker TR, Bernard HU, zur Hausen H: Classification of papillomaviruses. *Virology.* 2004;324: 17-27.
12. Franceschi S, Castellsagué X, Dal Maso L, Smith JS, Plummer M, Ngelangel C, et al.: Prevalence and determinants of human papillomavirus genital infection in men. *Br J Cancer.* 2002; 86: 705-11.
13. Nasca MR, Innocenzi D, Micali G: Association of penile lichen sclerosus and oncogenic human papillomavirus infection. *Int J Dermatol.* 2006; 45: 681-3.
14. Rubin MA, Kleter B, Zhou M, Ayala G, Cubilla AL, Quint WG, et al.: Detection and typing of human papillomavirus DNA in penile carcinoma: evidence for multiple independent pathways of penile carcinogenesis. *Am J Pathol.* 2001; 159: 1211-8.
15. Lont AP, Kroon BK, Horenblas S, Gallee MP, Berkhof J, Meijer CJ, et al.: Presence of high-risk human papillomavirus DNA in penile carcinoma predicts favorable outcome in survival. *Int J Cancer.* 2006; 119: 1078-81.
16. Bezerra AL, Lopes A, Santiago GH, Ribeiro KC, Latorre MR, Villa LL: Human papillomavirus as a prognostic factor in carcinoma of the penis: analysis of 82 patients treated with amputation and bilateral lymphadenectomy. *Cancer.* 2001; 91: 2315-21.

Dr. David M. Prowse

*Centre for Molecular Oncology, Institute of Cancer
Bart's and The London Queen Mary's School of
Medicine and Dentistry
John Vane Science Centre
London, United Kingdom
E-mail: d.m.prowse@qmul.ac.uk*